UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/648,089	08/26/2003	Samuel H. Gellman	09820.286	2777

25005 7590 02/01/2007

DEWITT ROSS & STEVENS S.C.
8000 EXCELSIOR DR
SUITE 401
MADISON, WI 53717-1914

EXAMINER	
KOSAR, ANDREW D	
ART UNIT	PAPER NUMBER
1654	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/648,089	GELLMAN ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6,8,9 and 11* is/are pending in the application.

4a) Of the above claim(s) *8,9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments/Amendments

Applicant's amendments and arguments filed November 6, 2006 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 4, 6, 8, 9 and 11 are pending.

Claims 8, 9 and 11 remains withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Any rejection and/or objection not specifically addressed is herein withdrawn.

Claims 4 and 6 are objected to for the following informalities: Claims 4 and 6 have been amended in the response of November 6, 2006, however the recitation, "and the substituents listed above for V and W" (preceding the 'strikeout') is extraneous and should have been deleted in the previous amendment.

Appropriate correction is required.

35 U.S.C. 101 reads as follows:
Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Applicant reiterates the arguments previously presented, specifically that Seebach provides utility for the instant claims and further argues that utility of the compounds of US

Patent 6,958,384 is "**identical**" (Remarks, page 20). Applicant readdresses the declaration of Dr. Gellman at length.

With regards to US 6,958,383, Applicant is kindly directed to MPEP § 716.07, which states in the first line, "Since every patent is presumed valid (35 U.S.C. 282), and since that presumption includes the presumption of operability (*Metropolitan Eng. Co. v. Coe*, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935), **examiners should not express any opinion on the operability of a patent**." (emphasis added). With regards to the instant application, the examiner respectfully disagrees that the instantly claimed compounds have utility under 35 USC § 101 and enablement under 35 USC § 112.

With regards to the declaration of Dr. Gellman and the further explanation of the purpose and content, the examiner appreciates the extensive discussion, but notes that it has been previously been considered and found not persuasive. Specifically, Dr. Gellman extrapolates the generic concept of foldamers inhibiting a generic protein-protein interaction to an experiment blocking Bcl-x_L/BH3 domain interactions. However, nowhere in the instant specification can the examiner find any reference to blocking Bcl-x_L/BH3 domain interactions. If such a reference were present, with adequate guidance on performing such an experiment- in the instant specification, the compounds would likely have a utility, as blocking blocking Bcl-x_L/BH3 domain interactions has a specific, substantial and credible utility. Additionally, Applicant's asserted utility (Remarks, page 31, last paragraph), is not within the instant disclosure, and thus cannot provide the utility.

With regards to "research tool" (Remarks, page 30, last paragraph), the examiner has reviewed MPEP § 2173.01(I)(C), and agrees that it is not "clearly delineated" as a basis for a

lack of utility. However, the preceding sentence, as stated below (and previously, "Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm." The 'research tool' designation, as intended by the examiner, is that the compounds, even as part of a library of compounds, must still be evaluated (further research) to determine their specific function. In ascertaining a specific function, one could ask the rhetorical question, "how many of the infinite number of compounds within the instantly claimed genus would one have to screen against the thousands (if not millions) of protein-protein interactions to determine a single interaction that is disrupted?" KIM (below) attempted to simply bind profilin with a peptide of the instant genus, without success.

Applicant is reminded that "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. *See Brenner v. Manson*, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.") Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. (*Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 42 USPQ2d 1001 (Fed. Cir. 1997)).

Claims 4 and 6 are/remain rejected under 35 U.S.C. § 101, for the reasons of record and those set forth below, because the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility.

Claims 4 and 6 are/remain rejected under 35 U.S.C. § 112, first paragraph (enablement), for the reasons of record. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth under 35 USC § 101, one skilled in the art clearly would not know how to use the claimed invention.

Because Applicant argues the rejection under 35 USC §§ 101 and 112, 1st paragraph, simultaneously, as the rejection under § 112, 1st paragraph, is predicated entirely upon the rejection under § 101, the examiner will address Applicant's remarks in kind.

Applicant previously argued at length that the compounds are supported by a credible, substantial and specific utility.

KIM (Y.J. Kim et al. Bioorg. Med. Chem. Let. (2000) 10, pages 2417-2419) provides further evidence to support the examiner's previously presented rejection and rebut Applicant's position that the utility of these compounds as claimed are well known, established and credible. Kim teaches βPro_{10}-Tyr, which is within the genus of the instantly claimed compounds (as discussed under 35 USC § 102, below). Kim examined "the possibility that β-peptide can substitute for the natural peptide" (page 2418) as a ligand of profiling and that it "failed to bind profiling, whereas the corresponding α-L-proline decamer bound tightly to this protein" (Abstract).

Here, Kim provides the possibility of studying the interactions, but determines *inter alia* that the probe is unsuitable, and thus it is inoperative. Without a probe, one cannot study the binding between two proteins.

With regards to Seebach, the Examiner considered the disclosure of Seebach to be inapplicable, as the compounds of Seebach are γ-dipeptides, while the instantly claimed

compounds are, at minimum, tetrapeptides with at least 1 α-amino acid and at least 2 cyclically constrained β-amino acids. The compounds are not coextensive or commensurate in scope, and thus cannot provide a 'well established utility' for the instant compounds based upon structure and amino acid content.

Furthermore, Seebach merely provides further evidence that the compounds are not of a well established utility, as even Seebach states that the results, "promise a potential of γ-peptides for the development of peptidase-resistant peptidomimetic drugs." (page 777, last paragraph). Seebach makes no reference or inference that the compounds relate to tetrapeptides (or larger) with α and cyclically constrained β-amino acids that are instantly claimed.

More recently, SCHMITT (M.A. Schmitt, et al. J. Am. Chem. Soc. (2005) 127, pages 13130-13131) teaches compounds which are of a similar structure to those of the instant application (e.g. compound 1). Schmitt, while not contemporaneous with the instant application, provides that the art still does not provide a 'well established' utility, as Schmitt teaches that, "Foldamers of this type [α/β-peptides] might mimic recognition surfaces on proteins and thereby disrupt specific protein-protein interactions [citing Sadowsky (2005)] or perform multifunctional catalysis of chemical reactions." (page 13131, last paragraph). These are general utilities, not specific as required by the statute.

Furthermore, while Applicant asserts that a compound library is a "useful endeavor" (page 20, *Remarks*), it does not meet the requirements of § 101, and thus § 112, 1st paragraph. Disruption of protein-protein interactions is a generic utility, and the questions that arise are, "which specific protein-protein interactions are contemplated and disclosed to be disrupted by Applicant?" and, "to what end are the interactions disrupted (e.g. increasing clot formation,

preventing angiogenesis, increasing milk production, etc.)?" The specification is silent to any specific protein-protein interaction that is disrupted or what is the effect of the disruption.

While chemical libraries are commercially available, they are sold as research tools, which are clearly delineated by MPEP § 2107.01(I) as being a utility which is not substantial (*see, e.g. page 7, Office Action mailed 5/4/05*). It is noted that the Exhibits do not discuss the particulars of the instant invention, e.g. examples of the instantly claimed compound, but rather generalizations on peptide libraries. Furthermore, as stated in the previous office action the MPEP states, "An assessment that focuses on whether the invention is useful only in a research setting thus does not address whether the invention is in fact "useful" in a patent sense. Instead, Office personnel must distinguish between inventions that have a specifically identified substantial utility and inventions whose asserted utility requires further research to identify or reasonably confirm." (Emphasis added; *see page 7, Office Action mailed 5/4/05*).

Furthermore, MPEP § 2107 (II)A(3) (the Examination Guidelines for the Utility Requirement) sets forth the test for determining a 'well established utility', stating, "If at any time during the examination, it becomes readily apparent that the claimed invention has a well-established utility, do not impose a rejection based on lack of utility. An invention has a well-established utility if (i) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties or applications of a product or process), and (ii) the utility is specific, substantial, and credible." (emphasis added). A 'well-established' utility requires that the utility is specific, substantial and credible, and not a 'general' utility, as is the case in the instant application because there is no specifically identified substantial utility and the invention requires further research and testing to

determine what specific protein-protein interactions may be disrupted with the compounds of the instant invention.

Claims 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

MPEP § 2163 states that, "[n]ew or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement. See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) (subgenus range was not supported by generic disclosure and specific example within the subgenus range); *In re Smith*, 458 F.2d 1389,1395, 173 USPQ 679, 683 (CCPA 1972) (a subgenus is not necessarily described by a genus encompassing it and a species upon which it reads)." Further, the MPEP states, "[w]hile there is no *in haec verba* requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure."

In the instant case, the newly presented claim limitations, R^{15} and R^{16} cannot both be hydrogen, has amended the scope of the claims to exclude a subgenus, specifically where R^{15} and R^{16} are both hydrogen. However, it is noted that the specification does not provide explicit, implicit or inherent disclosure for the exclusion of such a subgenus. Specifically, the disclosure, and examples therein, provide no examples of compounds where only one of R^{15} and R^{16} is not hydrogen, providing only compounds having unsubstituted βPro or ACHC as the sterically hindered β-amino acid.

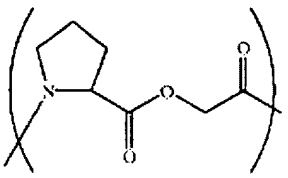
Furthermore, while Applicant relies upon MPEP 2173.05(i) and the citations therein, specifically "[the] specification, having described the whole, necessarily described the part remaining" (*In re Johnson* (558 F.2d 1008, 1009, 194 USPQ 187, 196 (CCPA 1977)), it does not apply in the instant application, as *Johnson* further states, "The notion that one who fully discloses, and teaches those skilled in the art how to make and use, a genus and numerous species therewithin, has somehow failed to disclose, and teach those skilled in the art how to make and use, that genus minus two of those species, and has thus failed to satisfy the requirements of §112, first paragraph, appears to result from a hypertechnical application of legalistic prose relating to that provision of the statute. All that happened here is that appellants narrowed their claims to avoid having them read on a lost interference count." (*Johnson* at 196). *Johnson* was excluding only two species, which were exemplified in the disclosure, and not a subgenus which is not described in the specification or examples.

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4 and 6 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record and those set forth below.

Applicant argues that the claim language is clear and definite, providing specific references to the specification and an exemplary analogy to cars on a parking lot.

While the examiner appreciates the analogy and agrees that the grammar of the instant claims is correct with regards to each/is, the examiner disagrees with the analysis that the claims are definite.

The claim preamble recites that each X or Z is an amino acid. The examiner understands the subscript identifies the multiple number for each X, e.g. X_2 is (X′)-(X′′), etc. and this is not the basis for the rejection. The rejection is with regards to the inconsistency between the later recitation of X or Z comprising an amino acid and the initial recitation that X or Z is an amino acid. It is highly unclear whether the positions describe a single amino acid, e.g. X is alanine, or whether X defines a dipeptide or polypeptide, e.g. X is Ala-Glu, which is consistent with the recitation that X comprises an amino acid. In the alternate definition of X comprising an amino acid could include such compounds as those having  as a structural element, as the compound comprises proline and a glycolic acid linker (e.g. Gellman US Patent 6,060,585).

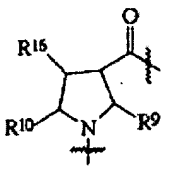
Claims 4 and 6 recite, "each X and each Z is independently variable and is selected from the group consisting of α-amino acid residues, β-amino acid residues, and γ-amino acid residues, provided that at least one X or Z comprises an α-amino acid residue and at least another two of X or Z comprise two cyclically constrained β-amino acid residues;..." (emphasis added) which is unclear and indefinite.

The claim does not allow for X and/or Z to 'comprise' anymore than a single amino acid, as the introductory recitation is that each X and each Z is..., while comprising allows for 1 or more amino acids, or other moieties, to be present at each position.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4 and 6 are rejected under 35 U.S.C. 102(b) as being anticipated by KIM (Y.J. Kim et al. Bioorg. Med. Chem. Let. (2000) 10, pages 2417-2419).

Kim teaches βPro_{10}-Tyr, which is within the genus of the instantly claimed compounds, being such that Z is an α amino acid, Tyr, and each of the 10 repeating X units is a βPro amino acid; βPro is an amino acid of the formula 

, where each R is H; each a, c and d are positive integers with a + c >3, being 10, 1 and 1 respectively (or any combination therein that would read upon Kim).

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

This application contains claims 8, 9 and 11 drawn to an invention nonelected with traverse on March 7, 2005. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 08:00 - 16:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia J. Tsang can be reached on (571)272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Andrew D. Kosar, Ph.D.
Patent Examiner
Art Unit 1654

JOHN LEGUYADER
DIRECTOR
TECHNOLOGY CENTER 1600

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600